Claims

1. An isolated nucleic acid molecule selected from the group consisting of:

(a) nucleic acid molecules which hybridize under stringent conditions to a molecule consisting of a nucleotide sequence set forth as SEQ ID NO:1 and which code for a MIVR-1 polypeptide having cardiac cell anti-apoptotic activity,

(b) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code, and

(c) complements of (a) or (b).

2. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises the nucleotide sequence set forth as SEQ ID NO:1.

3. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule consists of the nucleotide sequence set forth as SEQ ID NO:3 or a fragment thereof.

4. An isolated nucleic acid molecule selected from the group consisting of

(a) unique fragments of a nucleotide sequence set forth as SEQ ID NO:1, and

(b) complements of (a),

provided that a unique fragment of (a) includes a sequence of contiguous nucleotides which is not identical to any sequence selected from the sequence group consisting of

(1) sequences selected from the group consisting of SEQ ID NOs. 14-16, and 17,

(2) complements of (1), and

(3) fragments of (1) and (2).

5. The isolated nucleic acid molecule of claim 4, wherein the sequence of contiguous nucleotides is selected from the group consisting of:

(1) at least two contiguous nucleotides nonidentical to the sequence group,

(2) at least three contiguous nucleotides nonidentical to the sequence group,

(3) at least four contiguous nucleotides nonidentical to the sequence group,

(4) at least five contiguous nucleotides nonidentical to the sequence group,

(5) at least six contiguous nucleotides nonidentical to the sequence group, and

(6) at least seven contiguous nucleotides nonidentical to the sequence group.

6. The isolated nucleic acid molecule of claim 4, wherein the unique fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20, nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, and 200 nucleotides.

7. The isolated nucleic acid molecule of claim 4, wherein the molecule encodes a polypeptide which is immunogenic.

8. An expression vector comprising the isolated nucleic acid molecule of claims 1, 2, 3, 4, 5, 6, or 7 operably linked to a promoter.

9. An expression vector comprising the isolated nucleic acid molecule of claim 4 operably linked to a promoter.

10. A host cell transformed or transfected with the expression vector of claim 8.

11. A host cell transformed or transfected with the expression vector of claim 9.

12. An isolated polypeptide encoded by a nucleic acid molecule of claim 1, 2, 3, or 4, wherein the polypeptide, or fragment of the polypeptide, has cardiac cell anti-apoptotic activity.

13. The isolated polypeptide of claim 12, wherein the polypeptide is encoded by the nucleic acid molecule of claim 2.

14. The isolated polypeptide of claim 13, wherein the polypeptide comprises a polypeptide having the sequence of amino acids 1-287 of SEQ ID NO:2.

15. An isolated polypeptide encoded by a nucleic acid molecule of claim 1, 2, 3, or 4, wherein the polypeptide, or fragment of the polypeptide, is immunogenic.

16. The isolated polypeptide of claim 15, wherein the fragment of the polypeptide, or portion of the fragment, binds to a human antibody.

17. An isolated binding polypeptide which binds selectively a polypeptide encoded by an isolated nucleic acid molecule of claim 1, 2, 3, or 4.

18. The isolated binding polypeptide of claim 17, wherein the isolated binding polypeptide binds to a polypeptide having the sequence of amino acids of SEQ ID NO:2.

19. The isolated binding polypeptide of claim 18, wherein the isolated binding polypeptide is an antibody or an antibody fragment selected from the group consisting of a Fab fragment, a $F(ab)_2$ fragment or a fragment including a CDR3 region.

20. A method for determining the level of MIVR-1 expression in a subject, comprising measuring expression of MIVR-1 in a test sample from the subject to determine the level of MIVR-1 expression in the subject.

21. The method of claim 20, wherein the measured MIVR-1 expression in the test sample is compared to MIVR-1 expression in a control containing a known level of expression.

22. The method of claim 20, wherein the expression of MIVR-1 is MIVR-1 mRNA expression.

23. The method of claim 20, wherein the expression of MIVR-1 is MIVR-1 polypeptide expression.

24. The method of claim 20, wherein the test sample is tissue.

25. The method of claim 20, wherein the test sample is a biological fluid.

26. The method of claim 22, wherein MIVR-1 mRNA expression is measured using PCR.

27. The method of claim 22, wherein MIVR-1 mRNA expression is measured using Northern blotting.

28. The method of claim 23, wherein MIVR-1 polypeptide expression is measured using monoclonal antibodies to MIVR-1.

29. The method of claim 23, wherein MIVR-1 polypeptide expression is measured using polyclonal antisera to MIVR-1.

30. The method of claim 23, wherein expression of MIVR-1 is measured using MIVR-1 cardiac cell anti-apoptotic activity.

31. A method for identifying an agent useful in modulating cardiac cell anti-apoptotic activity of a molecule, comprising:

(a) contacting a molecule having cardiac cell anti-apoptotic activity with a candidate agent,

(b) measuring cardiac cell anti-apoptotic activity of the molecule, and

(c) comparing the measured cardiac cell anti-apoptotic activity of the molecule to a control to determine whether the candidate agent modulates cardiac cell anti-apoptotic activity of the molecule,

wherein the molecule is a nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d, or an expression product thereof.

32. A method of diagnosing a condition characterized by aberrant expression of a nucleic acid molecule or an expression product thereof, said method comprising:

a) contacting a biological sample from a subject with an agent, wherein said agent specifically binds to said nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof; and

b) measuring the amount of bound agent and determining therefrom if the expression of said nucleic acid molecule or of an expression product thereof is aberrant, aberrant expression being diagnostic of the condition;

wherein the nucleic acid molecule is at least one nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

33. The method of claim 32, wherein the nucleic acid molecule is at least two nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

34. The method of claim 32, wherein the nucleic acid molecule is at least three nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

35. The method of claim 32, wherein the nucleic acid molecule is at least four nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

36. The method of claim 32, wherein the nucleic acid molecule is at least five nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

37. The method of claim 32, wherein the condition is a cardiovascular condition selected from the group consisting of myocardial infarction, stroke, arteriosclerosis, and heart failure.

38. The method of claim 32, wherein the condition is cardiac hypertrophy.

39. A method for determining regression, progression or onset of a vascular condition in a subject characterized by aberrant expression of a nucleic acid molecule or an expression product thereof, comprising:

monitoring a sample from a patient, for a parameter selected from the group consisting of

(i) a nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, BTG-2, TIS-11d, and VDUP-1,

(ii) a polypeptide encoded by the nucleic acid molecule,

(iii) a peptide derived from the polypeptide, and

(iv) an antibody which selectively binds the polypeptide or peptide,

as a determination of regression, progression or onset of said vascular condition in the subject.

40. The method of claim 39, wherein the sample is a biological fluid or a tissue.

41. The method of claim 39, wherein the step of monitoring comprises contacting the sample with a detectable agent selected from the group consisting of

(a) an isolated nucleic acid molecule which selectively hybridizes under stringent conditions to the nucleic acid molecule of (i),

(b) an antibody which selectively binds the polypeptide of (ii), or the peptide of (iii), and

(c) a polypeptide or peptide which binds the antibody of (iv).

42. The method of claim 41, wherein the antibody, the polypeptide, the peptide or the nucleic acid is labeled with a radioactive label or an enzyme.

43. The method of claim 39, comprising assaying the sample for the peptide.

44. A kit, comprising a package containing:

an agent that selectively binds to the isolated nucleic acid of claim 1 or an expression product thereof, and

a control for comparing to a measured value of binding of said agent to said isolated nucleic acid of claim 1 or expression product thereof.

45. The kit of claim 44, wherein the control is a predetermined value for comparing to the measured value.

46. The kit of claim 44, wherein the control comprises an epitope of the expression product of the nucleic acid of claim 1.

47. The kit of claim 44, further comprising a second agent that selectively binds to an isolated nucleic acid molecule selected from the group consisting of IEX-1, VDUP-1, BTG-2, and TIS-11d, or an expression product thereof, and

a control for comparing to a measured value of binding of said second agent to said nucleic acid molecule or expression product thereof.

48. A method for treating a cardiovascular condition, comprising:

administering to a subject in need of such treatment an agent that modulates expression of a molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d, in an amount effective to treat the cardiovascular condition.

49. The method of claim 48, further comprising co-administering an agent selected from the group consisting of an anti-inflammatory agent, an anti-thrombotic agent, an anti-platelet agent, a fibrinolytic agent, a lipid reducing agent, a direct thrombin inhibitor, a glycoprotein IIb/IIIa receptor inhibitor, an agent that binds to cellular adhesion molecules and inhibits the ability of white blood cells to attach to such molecules, a calcium channel blocker, a beta-adrenergic receptor blocker, a cyclooxygenase-2 inhibitor, or an angiotensin system inhibitor.

50. A method of treating apoptotic cell-death of a cardiac cell in a subject, comprising:

administering to a subject in need of such treatment an agent that modulates expression of a molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d, in an effective amount to inhibit apoptotic cell-death of the cardiac cell in the subject.

51. The method of claim 50, wherein the subject has a condition selected from the group consisting of myocardial infarction, stroke, arteriosclerosis, and heart failure.

52. A method for inhibiting apoptotic cell-death of a cell, comprising:

contacting a molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d, with a cell under conditions that permit entry of the molecule into the cell, in an amount effective to inhibit apoptotic cell-death of the cell.

53. The method of claim 52, wherein the cell is selected from the group consisting of a cardiomyocyte and a vascular endothelial cell.

54. A method for treating a condition mediated by increased apoptotic cell-death of vascular endothelial cells in a subject, comprising:

administering to a subject in need of such treatment a molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d, in an amount effective to inhibit increased apoptotic cell-death of vascular endothelial cells.

55. A method for treating cardiac hypertrophy, comprising:

administering to a subject in need of such treatment an agent that increases cardiac cell-death, in an amount effective to treat cardiac hypertrophy in the subject,

wherein the agent that increases cardiac cell-death is an inhibitor of a nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d, or an expression product thereof.

56. A method for treating a subject to reduce the risk of a cardiovascular condition developing in the subject, comprising:

administering to a subject who is known to express decreased levels of a molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d, an agent for reducing the risk of the cardiovascular disorder in an amount effective to lower the risk of the subject developing a future cardiovascular disorder,

wherein the agent is an anti-inflammatory agent, an anti-thrombotic agent, an anti-platelet agent, a fibrinolytic agent, a lipid reducing agent, a direct thrombin inhibitor, a glycoprotein IIb/IIIa receptor inhibitor, an agent that binds to cellular adhesion molecules and inhibits the ability of white blood cells to attach to such molecules, a calcium channel blocker, a beta-adrenergic receptor blocker, a cyclooxygenase-2 inhibitor, or an angiotensin system inhibitor, or an agent that modulates expression of a molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

57. A method for identifying a candidate agent useful in the treatment of a cardiovascular condition, comprising:

determining expression of a set of nucleic acid molecules in a cardiac cell or tissue under conditions which, in the absence of a candidate agent, permit a first amount of expression of the set of nucleic acid molecules, wherein the set of nucleic acid molecules comprises at least one nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d,

contacting the cardiac cell or tissue with the candidate agent, and

detecting a test amount of expression of the set of nucleic acid molecules, wherein an increase in the test amount of expression in the presence of the candidate agent relative to the first amount of expression indicates that the candidate agent is useful in the treatment of the cardiovascular condition.

58. The method of claim 57, wherein the cardiovascular condition is selected from the group consisting of myocardial infarction, stroke, arteriosclerosis, and heart failure.

59. The method of claim 57, wherein the set of nucleic acid molecules comprises at least two nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

60. The method of claim 57, wherein the set of nucleic acid molecules comprises at least three nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

61. The method of claim 57, wherein the set of nucleic acid molecules comprises at least four nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

62. The method of claim 57, wherein the set of nucleic acid molecules comprises at least five nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

63. A method for identifying a candidate agent useful in the treatment of cardiac hypertrophy, comprising:

determining expression of a set of nucleic acid molecules in a cardiac cell or tissue under conditions which, in the absence of a candidate agent, permit a first amount of expression of the set of nucleic acid molecules, wherein the set of nucleic acid molecules comprises at least one nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d,

contacting the cardiac cell or tissue with the candidate agent, and

detecting a test amount of expression of the set of nucleic acid molecules, wherein a decrease in the test amount of expression in the presence of the candidate agent relative to the first amount of expression indicates that the candidate agent is useful in the treatment of cardiac hypertrophy.

64. The method of claim 63, wherein the set of nucleic acid molecules comprises at least two nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

65. The method of claim 63, wherein the set of nucleic acid molecules comprises at least three nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

66. The method of claim 63, wherein the set of nucleic acid molecules comprises at least four nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

67. The method of claim 63, wherein the set of nucleic acid molecules comprises at least five nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

68. A pharmaceutical composition, comprising:

an agent comprising an isolated nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d, or an expression product thereof, in a pharmaceutically effective amount to treat a cardiovascular condition, and

a pharmaceutically acceptable carrier.

69. The pharmaceutical composition of claim 68, wherein the agent is an expression product of the isolated nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

70. The pharmaceutical composition of claim 68, wherein the cardiovascular condition is selected from the group consisting of myocardial infarction, stroke, arteriosclerosis, and heart failure.

71. A pharmaceutical composition, comprising:

an agent that increases cardiac cell-death in a pharmaceutically effective amount to treat cardiac hypertrophy, wherein the agent that increases cardiac cell-death is an inhibitor of a nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d, or an expression product thereof, and

a pharmaceutically acceptable carrier.

72. A solid-phase nucleic acid molecule array consisting essentially of a set of nucleic acid molecules, expression products thereof, or fragments thereof, each nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d, fixed to a solid substrate.

73. The solid-phase nucleic acid molecule array of claim 72, further comprising at least one control nucleic acid molecule.

74. The solid-phase nucleic acid molecule array of claim 72, wherein the set of nucleic acid molecules comprises at least one nucleic acid molecule selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

75. The solid-phase nucleic acid molecule array of claim 72, wherein the set of nucleic acid molecules comprises at least two nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

76. The solid-phase nucleic acid molecule array of claim 72, wherein the set of nucleic acid molecules comprises at least three nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

77. The solid-phase nucleic acid molecule array of claim 72, wherein the set of nucleic acid molecules includes at least four nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.

78. The solid-phase nucleic acid molecule array of claim 72, wherein the set of nucleic acid molecules includes at least 5 nucleic acid molecules, each selected from the group consisting of MIVR-1, IEX-1, VDUP-1, BTG-2, and TIS-11d.